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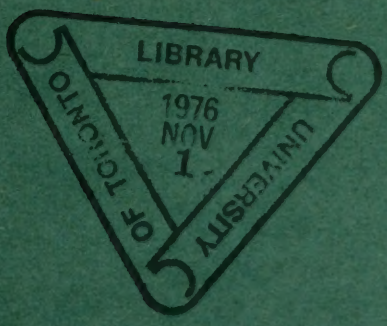
TRANSACTIONS

OF THE

SOCIETY OF TROPICAL MEDICINE AND HYGIENE.



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SOCIETY OF TROPICAL MEDICINE AND HYGIENE,
11, CHANDOS STREET, CAVENDISH SQUARE, W.

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MARCH, 1912.

VOLUME V. No. 5.

Proceedings of a Meeting of the Society on Friday, February 16th, 1912, SIR WILLIAM LEISHMAN, F.R.S., *President*, in the Chair.

Before proceeding to the business of the evening, the PRESIDENT proposed the following resolution with reference to the death of LORD LISTER, whose funeral had taken place in Westminster Abbey earlier in the day.

> The Society of Tropical Medicine and Hygiene, meeting on the day of the funeral of the late LORD LISTER, desires to place on record an expression of profound respect for the memory of one, who, in his generation, has contributed more to the progress of science in its application to the benefit of mankind than any other individual. The Society recognises that the practical connection traced by LORD LISTER between micro-organisms and disease laid the foundation for the work which is now being done by this and kindred societies in this same direction.

The resolution was carried unanimously.

The PRESIDENT next proceeded to welcome back the Vice-President, Sir HAVELOCK CHARLES, G.C.V.O., after his visit to India, and to congratulate him upon the high honour which had been conferred upon him by the King. He regarded it as an evidence of the gratitude of their Majesties for the excellent care which Sir Havelock must have taken to guard them from the dangers of a tropical climate.

The resolution was carried with acclamation, and Sir HAVELOCK CHARLES acknowledged the compliment which had been paid to him in a few suitable words.

THE CULTURE AND IDENTIFICATION OF THE GERM OF LEPROSY AND THE RELATIONSHIP OF THE HUMAN DISEASE TO RAT LEPROSY.

By H. BAYON,

Beit Memorial Research Fellow.

You are asked to decide this evening, as far as is possible in the short time at our disposal, whether the statements I shall make are justified or not. They are:—

(a)—The germ of leprosy can be cultivated from the lesions it causes in the human being.

(b)—Leprosy can be transmitted to animals, either after the culture of the germ or direct from the human being.

(c)—Rat leprosy and human leprosy are closely allied diseases; in fact the germ of both may be identical.

I intend to lay the whole weight of my arguments on the slides and microscopical sections being demonstrated. I therefore am unable to consider this evening much of the work done by others in the same field. I certainly shall do so in my next paper.*

The first projection shows the non-acid-fast and non-acid-resisting germ I cultivated from the nodules of a case of leprosy at the London School of Tropical Medicine. It is morphologically identical to the germ that KEDROWSKY got from his cases in Russia. You will note the peculiar way in which it has grouped itself round the original "bacilli." In other parts of the field it showed definite branching forms. It may be called an actinomycotic germ or a streptothrix, according to taste. It grew rapidly as a white viscid growth on placental-extract-glycerine-agar, and presented morphologically the peculiarities of a contaminating

* Results of cultures of the *B. Lepræ* have been recorded by the following:— 1882, GAUCHER ET HILLAIRET, HANSEN. 1886, NEISSER. 1888, BORDONI-UFFREDUZZI. 1889, BABES, GIANTURCO. 1890, STALLARD. 1891, KANTHACK, RAKE and BUCKMASTER. 1892, ABRAHAM, CAMPANA, DUCREY. 1897, E. LEVY, CZAPLEWSKY, STICKER and DIEUDONNÉ. 1898, SPRONK, TEICH. 1899, CARRASQUILLA, BARANNIKOW. 1901, KEDROWSKY, F. LEVY. 1902, VAN HOUTUN. 1903, GUEBERT, KLITIN, KARLINSKY. 1904, ROST, ZANONI. 1905, DEYKE and RESCHAD, WEILL. 1909, SHIGA, CLEGG, SERRA. 1910, DUVAL, ROST, WILLIAMS, TWORT. 1911, BAYON, BOECK. Unpublished results, FREMLIN (1904), HEWLETT (1910).

germ from the air. In my first paper on mentioning it I said that I feared it might not have anything to do with leprosy. The experiments I have since carried out with it have made me necessarily change my opinion. The stain used is ZIEHL-NEELSEN, the magnification is 1,000 diameters. (Fig 1).

The second slide shows the pleomorphic, diphtheroid-like organism cultivated on two different occasions from the nodules of the same case, also on placental-extract-glycerine-agar. Note its apposition to the original acid-fast "bacilli." This germ is acid-resisting — *i.e.*, after staining for ten minutes or more with warm carbol-fuchsine, it will resist the bleaching effects of 2 per cent. sulphuric acid for five seconds and not be stained by following treatment with dilute (1/10) Lœffler's methylene blue, but some of the germs will show then a clear ruby-red colour, and many others will be of a fainter red hue. Professor MUCH, who is present this evening, will, I hope, explain the cause of this stain reaction, from the standpoint of the presence of "nastin" in acid-fast germs. Note the branching forms and the clubbed shapes. This slide is also stained according to ZIEHL-NEELSEN, therefore the germs are blue. Magnification : 1,300 diameters. (Fig. 2).

The third projection is a coloured photo, according to Sanger-Sheppard's method, which has been very kindly taken for me by Messrs. Leitz. The magnification is 1,100 diameters, and I am sure you will admire the sharpness of the contours and the absolute precision of the colouring. This is the third or acid-fast stage of the germ, as it can be seen in the nodules of the leprous patients. Note the slightly thickened bacilli, identical in their morphology to those seen in the pus of lepers. (Fig. 3).

The germ at this stage is absolutely acid-fast—*i.e.*, after staining for three minutes with warm carbol-fuchsine it cannot be bleached even with 20 per cent. nitric acid in three minutes time, and will not stain blue after treatment with Lœffler's alkaline methylene blue. I must, however, remark that not all germs in a slide are equally acid-proof. This is, however, an observation that can also be made on cultures of any germ in its acid-fast stage. Incidentally I may mention that I do not consider that the property of being acid-proof sufficiently characterises any germ, as it is simply the appearance of a transitory condition in many cases I have investigated. Probably the same holds good for many more

I have not examined from this point of view, which however has already been most ably put forward by FOULERTON on various occasions.

What are my proofs that these three different conditions represent but the successive stages of HANSEN'S "bacillus," which is originally a filamentary branching, non-acid-proof organism?

First of all I must mention the work of KEDROWSKY, who, in 1901, expressed the opinion, based on experiments, that leprosy might be due to an organism possessing a developmental cycle similar to certain actinomycotic germs. Later on we have DEYCKE'S, ROST and WILLIAMS' work on the subject; moreover, HERMAN'S and ABRAHAM'S observation on the incomplete acid-fastness of HANSEN'S "bacillus" in young nodules.

Next I should refer to the experiments of SANFELICE, LOMBARDO-PELLEGRINO, CZAPLEWSKY, GRASBERGER, TOBLER, AUJETZKY, WEBER, NABARRO (these last as yet unpublished) on the varying degree of acid-fastness of various germs according to the media they have been cultivated upon or after passage through animals.

I should also mention the observations of BIRT and LEISHMAN, FLEXNER, KEDROWSKY, RABINOWITSCH, SILBERSCHMIDT, NOCARD, BERESTNEW, MOELLER, EPPINGER, SABRAZES ET RIVIÈRE, who have described acid-fast and partially acid-fast branching germs, in other words actinomycotic germs, capable of breaking up into acid-fast rods, from various sources.

As regards the diphtheroid stage we have GORDON'S study of a streptothrix which broke up into diphtheroids and which was cultivated from the throat of a child. Moreover, branching forms in diphtheroids have been seen by KLÆIN, FRÆNKEL (1895), BABES (1895), BERNHEIM and FOLGER (1896), SCHIWAN (1900). SPIRIG has on two occasions even got hyphæ in diphtheroids—an observation which I admit has not been generally accepted, though the fact is certainly not out of the realm of possibility.

Branching in tubercle has been repeatedly recorded: by ROUX ET NOCARD (1887), METSCHNIKOFF (1888), KLEIN (1890), MAFFUCCI (1892), FISCHEL (1893), BABES (1895), STRAUSS (1895), SCHIWAN (1900).

To persuade you, if necessary, that acid-resisting branching germs do exist, I will project a coloured micro-photograph of BIRT and LEISHMAN'S pathogenic streptothrix, stained according to ZIEHL-NEELSEN. This photo has been made by Dr. REID, of the Lister Institute, whom I

wish to thank for the trouble he has taken in the preparation of these lantern slides.

I am obliged, however, to keep myself to my own personal observations, and so I will project a colour-photo of the results I got by injecting the non-acid-proof branching germ into the peritoneal cavity of a rat. Three rabbits and one rat were injected. The rabbits died before any definite change could be observed, the rat developed a lump at the site of injection. This lump was punctured three months after inoculation and the juice showed leucocytes crammed with definitely acid-fast germs, which still had retained their "ray-fungus" habitus. I took a culture and that was the acid-fast germ I demonstrated as my third slide. The non-acid-fast germ had turned into an acid-fast "bacillus," and could now be cultivated as such. This culture is very similar to KEDROWSKY's strain, because it is a white, slow growing, peculiarly wrinkled organism, not at all unlike to avian tubercle.

I also injected the diphtheroid intraperitoneally into a mouse. After three weeks the mouse died and I was able to regain the germ as an acid-fast diphtheroid in sections and cultures. The culture was, however, contaminated by cocci and died out. The corresponding slides are under the microscopes. The lesions resulting in the peritoneal glands of the mouse were absolutely identical to those seen in spontaneous rat leprosy, as regards staining reaction, position and quantity of "bacilli."

My next projection relates to the lesions resulting from the injection of the germ in its acid-fast stage. This is the spleen of a mouse, seven months after it had been injected intra-peritoneally with 0·3 of an emulsion of KEDROWSKY's strain. The liver also showed similar lesions. These enormous red patches consist all of acid-fast bacilli, which have hardly given rise to any inflammatory reaction, showing, therefore, their low toxicity. You will admit that the analogy with human and rat leprosy is most striking. (Fig. 6).

This is a section from the lung of the same animal. Note the absence of caseation, the minimum inflammatory re-action, the non-appearance of giant cells of the LANGHAN's type, the absence of sclerosed vessels, all details which help to distinguish HANSEN's "bacillus" from its near relation, the tubercle. These slides should prove that a non-acid-resisting branching germ is capable of acquiring acid-proof properties after injection into animals, that it can then be regained by culture

as an acid-fast rod, and that it can cause lesions extremely similar to those occuring in leprosy of the man and rat. Whether this germ is HANSEN'S "bacillus" or not, I shall prove by other independent methods.

So far my work had but been the confirmation of the results of KEDROWSKY. I thereupon undertook to continue the work to a definite conclusion. Acid-fast germs are absolutely ubiquitous, they have been found practically everywhere where they have been carefully looked for, in dung, in earth, in tap-water. I am demonstrating one of these tap-water acid-fasts taken from the tap in my room at the Lister Institute. In the same water I encountered amœbæ of the verrucosa type, which contained acid-fasts, as also did, but to a much lesser extent, the Euplotes sp. which swarmed in the mould growing round the tap.

On the table you see racks with over forty different strains of these acid-fasts, the great majority of which have been found in milk. Fourteen of these germs I owe to the kindness of Dr. NABARRO, who has isolated them himself.

You see, therefore, that it is absolutely necessary to identify any acid-fast or other germ cultivated from one or several cases of leprosy before stating its relationship to HANSEN'S "bacillus." Professor KEDROWSKY having kindly put one of his strains at my disposal, I set to work distinguishing it from the three germs it might be, viz.: human tubercle, smegma or avian tuberculosis. I determined to find a series of tests that would enable me to identify any germ I might get and to definitely state whether it had anything to do with HANSEN'S "bacillus" or not.

By means of intravenous injection of the common smegma "bacillus" I produced the clinical features of leprosy in the rabbit, as described in previous papers of mine. The nodules in the skin, in the kidney, showed enormous felt-like masses of acid-fast germs which you see in this section. There is sufficient resemblance to the lesions produced by HANSEN'S "bacillus" to enable an unskilled or even enthusiastic worker to claim he had produced the identical lesions of leprosy by the injection of some common saprophytic acid-fast, such as the smegma germ. (Fig. 5).

However, we know that the germ of leprosy belongs to the "tubercle" group, as has been confirmed (after the histological evidence had given several valid reasons for this view) by means of serological tests by MUCH and HŒSSLI, and also WILLIS. On injecting KEDROWSKY'S

strain intravenously into rabbits, I soon found that it caused lesions extremely similar to those caused by the intravenous injection of the avian tubercle into the same animal. You will notice the similarity caused by the "ray-fungus" like disposition of the organisms (which, however, can also be produced by the human variety of tubercle and by the timothy grass acid-fast germ [SCHULZE, LUBARSCH, ABBOT and GILDERSLEEVE]) in the two slides I am projecting.

My first step was, therefore, to exclude that the strain was tubercle, human or avian. I soon found that it was non-pathogenic for guinea-pigs, and that fowls could be injected with half a slope without showing any lesions on autopsy two months afterwards. It was absolutely necessary to carry out these experiments because under circumstances even human tubercle is capable of causing on injection into rabbits, lesions very similar to leprosy.

This is a specimen demonstrating the enormous quantity of bacilli which have accumulated in a nodule in the cœcum of a rabbit, which was injected intra-peritoneally with a full slope of human tubercle "bacilli," which had been heated for an hour at 60° C. You will see that the whole field is red with them. The similarity to leprosy is striking, but the germs are much more scattered about than is the case in leprosy, where the "bacilli" are more apt to congregate in groups.

Having persuaded myself that the germ cultivated from lepers was not an avian or other tubercle, as its appearance and lesions it caused in rabbits might well lead one to believe, I determined to test the serum of lepers against the acid-fast stage of this organism by means of the complement fixation method.

I prepared my antigen by alternately freezing and rapidly thawing an emulsion of "bacilli" in distilled water, with the intent of bursting, if possible, the waxy capsule which appears to envelop most acid-fast germs.

In each complement absorption test I put up at least four rows of tubes and never tested a germ by itself, but always in the same time as some other closely allied acid-fast germ. This method has been most successfully made use of by H. R. DEAN in distinguishing various allied strains of the para-typhoid group. In each row I diluted my serum 1/5, 1/10, 1/20, 1/40, 1/80, and so forth. In the first row, however, I made use of the antigen in full dose, in the second I linked up the serum with

half doses of antigen, in the third with quarter and in the fourth with one-eighth of the quantity used in the first row, the dilution being carried out with saline.

I made several experiments which enabled me to distinguish quite clearly avian from human tubercle with appropriate sera. However, here I am only concerned with giving my results as regards leprous serum.

These are the results obtained by linking the serum of a leper from Mauritius with KEDROWSKY's and DUVAL's strain of leprosy.

In the first row KEDROWSKY's strain reacted up to 1/160.

In the second row up to 1/40 to 1/80.

In the third row 1/20 to 1/40.

In the fourth row 1/10 to 1/20.

DUVAL's germ gave following results, viz :—

In the first row it reached up to one in 1/5 to 1/10.

In the second row slightly 1/5. All others negative.

In another experiment I tried KEDROWSKY's and ROST's strain against one other, using the serum of a patient, for which I have to thank Sir ARTHUR DOWNES and Dr. ABRAHAM. These are the results in one case :—

Dilution of serum 1/8, 1/16, 1/32, etc.

KEDROWSKY's germ.

In the first row reacted till 1/64.

In the second row 1/32.

In the third row 1/16. The same in the fourth row.

ROST's germ.

Dilutions of serum 1/7, 1/14, 1/28, etc.

In the first row 1/7 to 1/14.

In the second 1/7. All others negative.

I will mention that results agreeing with these, as far as the specificity of KEDROWSKY's germ is concerned, have been arrived at by Dr. HUNT, at St. George's, by means of the opsonic index test. Dr. LEDINGHAM found a very high tropin-content against KEDROWSKY's germ in the inactivated serum of a patient who had received several injections of bacterial extract of KEDROWSKY's strain of leprosy.

These experiments, taken together with the slides I have shown you ought to warrant the claim that the germ has been identified, and that if it had been a contamination of some sort, it would not have fulfilled

all the conditions it has done so far, including that of giving a tuberculin-like reaction on injection as a bacterial extract made on the lines of KOCH'S Alt-tuberkulin. I cannot, however, give too much value to this test by itself, as it is not sufficiently specific to my mind.

The conclusion that I therefore draw is that KEDROWSKY'S germ is indentical with HANSEN'S "bacillus" because it has repeatedly been cultivated from lepers, because it causes leprous lesions in rats and mice, and last, but by no means least, because it reacts specifically with the serum of lepers in a way that neither tubercle or avian do. Moreover it is not identical with any other known germ.

My culture is morphologically identical, to the naked eye and under the microscope, to this strain. It grows at the same rate, in the same fashion on the same media, therefore I take it it is also leprosy, though I have not been able, so far, to put it through all the tests necessary for its identification.

The next question to solve is whether leprosy can be transmitted to the common laboratory animals, the rabbit, rat, mouse, direct from the human being, without first culturing the germ. I have published a paper on the subject in the *British Medical Journal* of February 24th, and do not wish now to go over the same ground again. I will simply project a photograph of the results obtained in rats and can only refer to the slides under the microscope. Regarding rabbits I will remark that the similarity of the resulting lesions to those of tuberculosis, made them not be recognised as leprosy and gave rise to the view that the authors who had published positive results had sown leprosy and reaped tuberculosis. There can now not be much doubt that the results of MELCHER and ORTMANN, WNOUKOW, WESENER, STANZIALE, and possibly also THIROUX were true leprosy. In all these animal experiments we must, however, prepare ourselves to have long series of incomplete or negative results.

Now to the question of rat leprosy. It is well known that the last leprosy conference after discussing the matter at length came to the conclusion that the human and rat disease had nothing to do with each other.

In my very first paper on leprosy I stated that I considered both diseases to be either identical or closely allied as human is to bovine tuberculosis because:—

(a)—The lesions in both diseases are microscopically identical (Fig. 4).

(b)—Because GEORGE DEAN found that:—

(1) The serum from a case of human leprosy agglutinated the acid-fast bacillus from the rat. Normal human serum had no agglutinating power.

(2) The serum of rats inoculated with the acid-fast bacilli agglutinated the diphtheroid DEAN cultivated from leprous rats. Normal rats' serum did not agglutinate the diphtheroid.

(3) Normal human serum and the serum from a tuberculous patient failed to agglutinate the diphtheroid, whereas the serum from a case of leprosy had distinct agglutinating properties.

To this evidence I am able this evening to add a further argument in favour of both diseases being very closely related. We have succeeded in cultivating from a case of rat leprosy, an acid-fast germ very similar to the one got from human leprosy.

Dr. LEDINGHAM having kindly got me some nodules from leprous rats, found in the course of plague investigations, I inoculated the ground up material, after treating it for a short time with 1/20 antiformin, intravenously into a rabbit and intra-peritoneally into a rat. The rabbit is still alive, five months after injection, but reacts in a complement absorption test up to 1/60 with human leprosy antigen.

The rat was killed one month after inoculation and showed the naked eye changes in the epiploon, *i.e.*, nodules, which have been described by DEAN in the disease. With the help of Dr. MARTINEZ, cultures were attempted on several tubes of fish-juice-glycerine-agar. Only one culture was successful, out of a dozen attempted and that was with juice from the spleen. After a month incubation at 37°C., small pinhead size, scattered ivory-beaded colonies appeared. These consisted of acid-fast rods. They were sub-cultured and you see the result on the table: a white wrinkled growth, very similar to human leprosy and therefore also not unlike to avian tuberculosis. Under the microscope they are short plump rods, absolutely acid-fast.

I am going to identify the germ in course, but in view of the various specimens I have shown this evening I think I am justified in considering it to be very probably rat leprosy. The microscopical appearances in the liver, spleen, omental nodules from the rat from which the culture was taken tended to show that a multiplication of the germs had taken place, however, not to a very marked extent.

ILLUSTRATIONS.

Fig. 1.—Culture on horse-serum-nutrose-agar, from nodules of case of leprosy at the London School of Tropical Medicine. Stain: ZIEHL-NEELSEN. Magnification: 1,000 diameters. Drawing by M. RHODES.

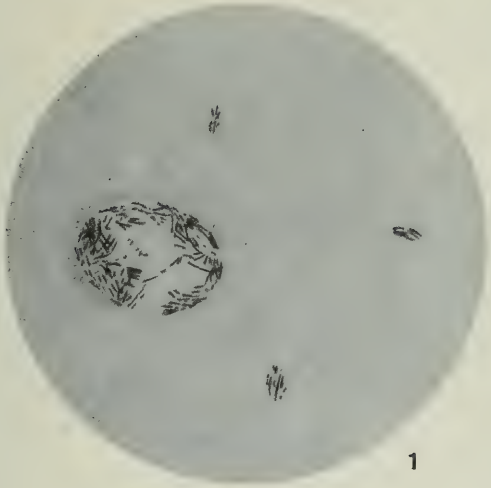
Fig. 2.—Diphtheroid-like pleomorphic organism from same case. Third sub-culture one month on placental-extract-glycerine-agar. Possibly a slight multiplication of the acid-fast bacilli may have taken place. Stain: ZIEHL-NEELSEN. Magnification: 1,300 diameters. Composite drawing from various parts of slides by M. RHODES.

Fig. 3.—Last or acid-fast stage of the actinomycotic germ of leprosy. Pure culture, two months' growth on fish-juice-glycerine-agar. Stain: ZIEHL-NEELSEN. Magnification: 1,100 diameters. From a coloured photo according to SANGER-SHEPPARD'S method, by Messrs. E. LEITZ.

Fig. 4.—Section of omental nodule from leprous rat, found in Ipswich by Drs. PETRI and MACALISTER. Stained according to ZIEHL-NEELSEN. Magnification: 500 diameters. Drawing by M. RHODES.

Fig. 5.—Lesions produced in kidney of rabbit by intravenous injection of MOELLER'S smegma germ. Stained according to ZIEHL-NEELSEN. Magnification: 300 diameters. Drawing by M. RHODES.

Fig. 6.—Lesions produced in spleen of mouse after intra-peritoneal injection of acid-fast stage of human leprosy germ. Stained according to GRAM. Purple masses consist of acid-fast, gram-positive bacilli. Magnification: 400 diameters. Colour photo according to SANGER-SHEPPARD, by Messrs. E. LEITZ.



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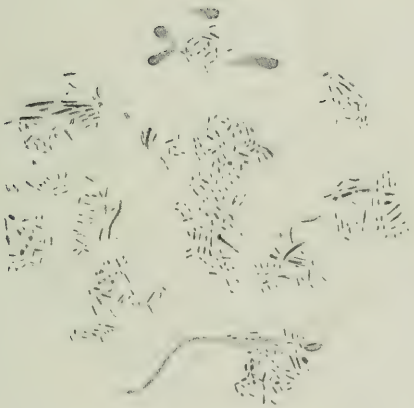

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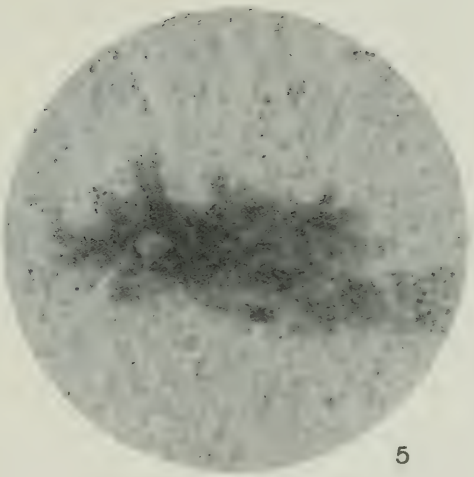

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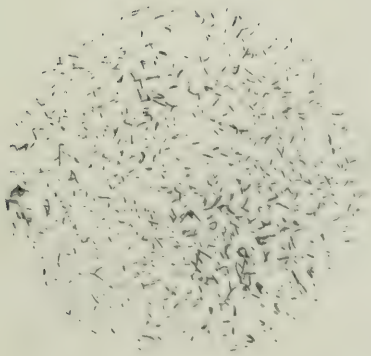

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ILLUSTRATIONS TO ACCOMPANY Dr. BAYON'S PAPER.

What are now the conclusions to be drawn from a clinical stand-point of view in relation to the observations I have recorded? I believe that my experiments entitle me to say that to all appearances the acid-fast stage of HANSEN'S "bacillus" is very slightly infective, because you have to inject relatively heavy doses to get definite, progressive lesions. On the other hand, the non-acid-proof conditions are more apt to cause the disease, even if the incubation period may be very long.

This leads me up to state that I believe that the early and progressive stages of leprosy are the only ones that are dangerous from an infective point of view.

How does this agree with clinical observations?

Though very slow in multiplying and exceedingly quiescent, the acid-fast "bacilli" are capable of resisting, at least as far as their morphology is concerned, thermic, chemical and physical influences to a very considerable extent. Under the microscope you will see some morphologically intact "bacilli" which have been boiled in ether for six hours at a stretch. I can show similar slides after drying, grinding and then boiling for twenty-four hours. This explains the fact that we never have any proof whether the "bacilli" in a lesion are capable of multiplying or not till we have definitely seen them do so in an animal or on media. Morphologically intact, faultlessly staining bacilli in a leprous nodule may be dead as an autoclaved culture, though of course death and life in relation to germs are certainly not such hard-and-fast distinctions as is the case with vertebrates.

I believe that an organism incapable of multiplying may still be able to eliminate toxines and in determining this exact point, we may open up the possibility for therapeutic treatment.

The analogy, if not identity of human and rat lepra, ought to enable us to throw light upon the way leprosy is transmitted, and therefore put us in condition to tackle the scourge amongst human beings from the standpoint of prevention.

These investigations were begun at the London School of Tropical Medicine, and then continued at the Lister Institute, and I desire to express my indebtedness to Sir PATRICK MANSON and Dr. MARTIN, and the Staff of both Institutions for the help and advice they have given me.

TREATMENT OF LEPROSY BY NASTIN, AND RESULTS SO FAR OBTAINED BY THIS TREATMENT.

By Professor GEORG DEYCKE, M.D., Hamburg.

I consider it a great pleasure to have the opportunity to read before this Society of specialists for tropical diseases a paper on the results which have been obtained by a method introduced by me, a few years ago, into the therapy of leprosy. It will be known to you, I think, that the treatment consists of the application of a neutral bacterial fat, which I called *nastin*, owing to its compact wax-like constitution (nastin from the Greek word, " nastos," which means compact).

Though I propose to deal to-night chiefly with practical data and facts, I may here briefly glance at some theoretical points. Nastin was first isolated from acid-fast streptothrices, which I cultivated from a case of tubercular leprosy, and vaccines obtained from the cultures of these streptothrices sufficed to cause very distinct reactions in cases of leprosy. At first, therefore, I thought that success in bringing this micro-organism into generic connection with the real leprosy bacillus was possible or even probable. This hypothesis, however, I very soon abandoned, and my work is therefore now in contrast with that of some other investigators who subsequently cultivated more or less acid-fast bacilli, and who, experimenting with these bacilli, have made observations similar to my own.

By extended experiments on men I found that the reactions obtained with the vaccines which I used at that time were caused by two different factors. Some of the reactions were no doubt, in a clinical sense, of a specific nature, *i.e.*, these reactions were confined to the leprous tissue and reacted favourably on the leprous process. But I also found that in other cases the reaction could not be specific, for no beneficent influence on the symptoms of the disease could be observed, although very violent reactions of a general nature occasionally took place.

In the course of further investigations I found that the specific and favourable reactions were bound to the acid-fast phase of the cultures; I concluded, therefore, that they depended on fatty substances, and I was finally able to show that amongst these the neutral fat, viz., the nastin,

was the active and curative constituent. The non-specific reactions are caused by bacterial albumens, and they are nothing else but symptoms of anaphylaxis, which are injurious and dangerous, especially if caused repeatedly.

I consider it, however, wrong in principle to conclude from such reactions that my streptothrices are identical or even congeneric with the real exciting cause of leprosy. The reactions caused by the bacterial albuminous bodies are due to anaphylaxis, but they are not at all of a specific nature, while the reactions caused by fatty bodies are specific in a therapeutic sense; from a biological point of view, however, they can be considered as specific of a group only in so far as certain substances may be common to a whole group of bacilli.

Moreover, I have proved for the bacillus tuberculosis, chemically and experimentally, that it contains nastin-like fats, which can replace the genuine nastin therapeutically, and this fact has been confirmed and extended by investigations made in the Institute of Dr. Much, Hamburg. We also know now that other acid-fast bacilli, which have no connection with the leprosy bacillus, possess nastin-like reactive neutral fats.

Recently Capt. Beauchamp Williams, I.M.S., has also observed reactions after the use of vaccines made from a streptothrix cultivated by him, and he claims a generic connection between this streptothrix and the bacillus lepræ (Hansen). As I have explained, I do not think this is possible, but except on this one point the report of Williams fully confirms each and every one of the observations which I made years ago with my own cultures of streptothrices. Perhaps the most important and interesting of all these newer observations is the fact that Capt. Williams also found that it was only the acid-fast phase of his streptothrix which was an efficient vaccine. You will see that here also the curative effect is very closely related to the fatty constituents.

The second theoretical point to which I wish to devote a few words is the question: How is the action of nastin on the leprous process produced? I have already repeatedly pointed out that the injections of nastin initiate, facilitate and accelerate the bacteriolytic destruction of the leprosy bacilli, which, of course, may happen sometimes spontaneously. This, too, has been confirmed by other authors. For, although I considered from the beginning that nastin itself was a bacteriolytic immune body, and although I had named it accordingly,

the true light in which to regard its action has been supplied only recently by the valuable serological investigations of Dr. MUCH and his school. I will briefly refer to four points in these researches which are of importance:—

(1) Immunising effects against acid-fast bacilli depend on the sufficient presence of partial anti-bodies, which represent nothing else but products of reaction to the partial antigens of the acid-fast bacilli; in other words, to their albumin bodies, lipoids, fats, etc.

(2) Nastin and other nastin-like neutral fats are real antigens, for they are able to produce anti-bodies; but they differ from the others, especially from the albuminous antigens, in that it has not been possible so far to produce anti-bodies with them in healthy men and animals. The formation of anti-bodies, however, is possible in leprous patients, provided the other partial anti-bodies are present.

(3) In leprosy the fat anti-bodies are not present at all or not in sufficient quantity, while the others, especially the albuminous anti-bodies, are found in a sufficient quantity in most or, at least, very many of the cases.

(4) If nastin is injected into a leprous patient, in whom the fat anti-bodies alone are absent, then we have the conditions under which the fat anti-bodies, which were not present, can be formed. And if this is the case, the circle of immunity is complete, and therefore we have immunisation, which, in our case, is a bacteriolytic effect.

This theory, founded by Dr. MUCH, is based not only on numerous biological and clinical experiments, but it also satisfactorily explains the inconstancy of the therapeutical action in different cases of leprosy. Anyone who has practised the nastin treatment of leprosy for some time will have observed these fluctuations. While some patients exhibit distinct evidence of therapeutic results or reactions after small doses, others do not show the effect of nastin until after a longer period of treatment, and others, again, are perhaps completely refractory. The only possible conclusion is that this difference in reaction depends on the ability of the lepers to respond to the nastin injections by the formation of fatty anti-bodies.

If you will allow me, I will now leave the territory of theory and come to discuss the practical results which have been obtained by nastin treatment.

In statistics which I have recently published, and which could be already considerably extended, I have compared in all 529 cases of leprosy treatment by nastin. In the total number I have not included :—

(1) Any cases of leprosy treated by me personally. I did this in order to keep to facts as far as possible. The fate of a new therapeutic treatment rests in the field of general medical practice and not in the hands of the discoverer.

(2) All cases treated in British Guiana, at first by me and later on by the Government Medical Officers. I do not include these cases because I have no statistics of the actual results. I can only tell you that most of the patients in the Mahaica leper asylum were in an extremely bad condition as regards their disease, and still a good number of them were discharged after they were examined bacteriologically and declared free from bacilli.

With these two exceptions I have included everything in my comparative statement that was at all within my reach. The material I have drawn from two sources. First, from the published reports that have reached me, and here I have every reason to assume that hardly anything has escaped me. Secondly, from interrogatories which I addressed at the end of 1910 to all the doctors who, so far as I could hear, had made practical use of the nastin treatment of leprosy.

In the first of the two following tables you will find the total number of all cases of leprosy treated by nastin. In the second I have grouped the cases according to the three prevailing manifestations of leprosy—the tubercular, the anæsthetic, and the mixed forms, although, partly on account of the want of exact statements, I was unable to classify all the cases. However, the material in these tables is ample enough to give a sufficiently clear illustration.

Before I go into these statistics, I beg to say that the headings (cured, nearly cured, considerably improved, improved, not improved or worse, dead), are not of course based on my own opinion, but on the statements of the doctors who treated the cases. It will be equally clear why I have refrained from any critical examination of the material. I have also included even such cases as in my opinion were quite inadequately treated, either for an insufficient time or contrary to my instructions, and on that account were, I consider, certain to give a negative result.

I may also mention that no fewer than sixty-nine medical men took part in the treatment of the cases of leprosy I have collected, and that the patients came from all parts of the world, indeed from almost every country in the world where leprosy is found at all.

TABLE I.

Total number of cases treated by Nastin.	Cured.	Nearly cured.	Considerably improved.	Improved.	Not improved or worse.	Dead.
529	13	34	131	154	192	5
	332 = 62·76 per cent.				197 = 37·24 per cent.	

TABLE II.

Among 424 cases treated there were—			Cured.	Nearly cured.	Considerably improved.	Improved.	Not improved or worse.	Dead.
Tub.	Anæsth.	Mixed.						
219	—	—	5	8	62	64	76	4
			139 = 63·47 per cent.				80 = 36·53 per cent.	
—	132	—	5	14	34	35	44	—
			88 = 66·67 per cent.				44 = 33·33 per cent.	
—	—	73	1	7	24	14	26	1
			46 = 63·01 per cent.				27 = 36·99 per cent.	

And now the figures may be considered. I begin with the second table, and please observe, in the first place, that the different forms of leprosy react in a very similar manner to nastin. The small percentages of deviation are of slight account. Personally, I am much struck by this statistical fact, for, from my personal experience and impressions, I should have expected that the tubercular and the mixed forms would turn out worse, but, above all, that pure anæsthetic leprosy would show a much more distinct advance on tubercular leprosy. Perhaps I was mistaken, through having seen and treated on the whole

more cases of tubercular than of nerve leprosy. Perhaps, however, it is partly due to other circumstances. I mean that in anæsthetic leprosy, which apart from its terrible mutilations appears to be the least severe form, we are too easily tempted to expect too much from the treatment. Where nerve tracks are entirely destroyed symptoms of functional decay must be permanent, even if the infected process is entirely cured. It is, therefore, sometimes very difficult to prove actual improvement in nerve leprosy. At any rate, it requires very exact comparative neurological examinations, which are always unsatisfactory, and frequently, in the case of coloured patients, are quite impracticable. But those who have had the opportunity of treating intelligent persons of the white races for nerve leprosy by nastin, have found in their case that there is little difficulty in demonstrating a progressive improvement. Moreover, in the nervous form of the disease, a great advance has already been made if we succeed in arresting the extension of the leprous process to fresh nerve centres. From this standpoint I think that, contrary to statistics, nerve leprosy will yet be found especially suitable for the nastin treatment.

Now as to the first table. In forty-seven cases the patients treated are reported as cured or nearly cured. I must, of course, leave the responsibility for these reports to the physicians who treated the cases, but I do not for a moment doubt the correctness of their judgment, more especially so as many doctors have proved their statements by careful bacteriological investigations, some of which could be repeated after long intervals, with the same negative result, *i.e.*, the proof of freedom from bacilli; and further, as a large number of these patients were discharged from Government leper asylums.

There is, however, one very pertinent observation that cannot be omitted. I have often asked myself whether and in what way it is possible objectively to demonstrate a perfect cure in leprosy. So far I have not been able to give a satisfactory answer to this question. By the ideal cure of an infectious disease we can only understand the condition in which the last disease organism has been destroyed and removed. This can hardly ever be proved in leprosy. But is this postulate better satisfied in other chronic infectious diseases? Leprosy, especially, should make us cautious in our assertions. I hold it advisable to speak in special cases of nothing more than temporary freedom from bacilli; and in the light of this expression, to introduce into legislation con-

cerning leprosy, the possibility of provisional discharges from the isolation hospitals in such a way as to allow of further observation and controlling examination.

Yet even with this restriction, made essentially for practical reasons, the qualitative results of the nastin treatment as shown in my statistics, are very satisfactory. I admit frankly that in this respect they far surpass my own expectations. I lay stress upon the fact that in my publications and lectures I have never spoken of a "cure" for leprosy, but always of "arrest of the disease," "improvement of the symptoms and of the general health of the patients." To prevent further misrepresentation, I may repeat here a few words spoken by me at the second International Leprosy Congress in Bergen (1909). From them you will see how I have formulated my opinion as to the therapeutic action of nastin.

"The nastin treatment, if consistently and rationally applied for a sufficient length of time, produces in a large percentage of cases of leprosy more or less extensive improvement in the leprous systems and in the general condition of the subjects."

You thus see that I attach less importance to the qualitative effects of nastin than to the quantitative results. This applies also to my first table, and renders it of greater import in forming an opinion regarding the method. It shows that in about 37 per cent. of all the cases no result or a negative one was obtained by nastin, while in 63 per cent. there was a positive result. I think, therefore, that I am justified in saying that nastin has quantitatively proved equal to the claims I made for it, and to the measure of its value which I gave as a guide for practical work; and I may here say that I am very glad to be able to give you to-night these statistics. Nobody realizes better than myself that nastin is no wonder-remedy. On the other hand I shall feel more than satisfied if after to-night's lecture you are convinced that the outlines and limits of nastin treatment can be strictly defined, both theoretically and practically.

Those of us who are in actual and constant touch with the problems of life, and medical men in a special sense belong to this class, are in therapeutics content with a progress which, although only moderate, is still within the limits of possibility. At the same time with better knowledge and more complete methods it should be possible in time to solve these problems definitely and completely.

SEROLOGICAL AND EXPERIMENTAL STUDIES ON LEPROSY.

By HANS MUCH, M.D., HAMBURG.

I.

Like those of tubercle, the bacilli of leprosy stand out prominently in the system of acid-fast organisms because of their pathogenic qualities. Further, a definite relation appears to exist between leprosy and tuberculosis, as well as between their bacilli and other acid-fast bacilli which are non-pathogenic for man. This was demonstrated in my Institute by MUCH, HÖSSLI, LESCHKE and DEILMANN, and, only a short time ago, Dr. WILLS has confirmed and published our results in English. We were able to show—chiefly by the reactions of immune bodies—a relationship between tubercle and lepra bacilli and other acid-fast bacilli which is due to inherent qualities common to all these organisms. Thus, tuberculous and tubercle-immunised persons responded to the reaction of complement-fixation, not only with tubercle, but also with other acid-fast bacilli, though not equally with all, and with certain sorts more than with others. A table which I have prepared shows the quantitative differences in these reactions, and according to this table the lepra bacilli have the closest resemblance to the tubercle bacilli.

In the same way leprous sera react not only against lepra bacilli, which we obtained from leprous tubercles, but they give also a specific reaction in the same scale of relationship with tubercle and other non-pathogenic acid-fast bacilli. These reactions are absolutely specific, although I am unable to demonstrate that point fully to night as time is insufficient. I must ask you therefore to look it up at your leisure in my publications and in those of my collaborators.

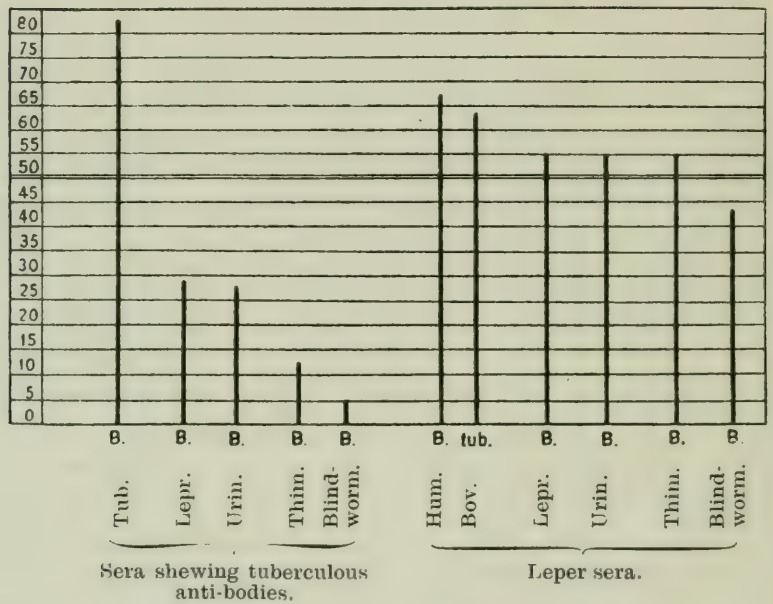
Not only do these complement-fixation tests show a kinship between leprosy and tuberculosis, but the same thing is true of the anaphylactic tests. Moreover, it is known that lepers react to tuberculin, but in a different way to tuberculous patients. And further, DEYCKE has since shown that the neutral fat nastin produces the same specific reactions, not only with leprous but also with tuberculous patients. A similar

neutral fat, prepared from the tubercle bacillus, which, I may say, is very hard to obtain, causes specific reactions both with leprous and tuberculous persons.

TABLE A.

Centralbl. f. Bakt. etc. I. Abt. Originale. Bd. 61. Heft 1/2.

Complement-fixation with acid-fast bacilli.



II.

Now it is questionable whether the relationship between leprosy and tuberculosis depends on one specific substance or on several. But numerous investigations appear to indicate that it depends on several factors. By splitting up tubercle bacilli, and determining the arrangement of their chemical constituents, we find that they are composed of three great groups :—

(1) Albuminous substances.
(2) Neutral-fats combined with a fatty alcohol.
(3) A mixture of fatty acids and lipoids.

Lepra bacilla have the same chemical qualities ; therefore, although unable to grow them in artificial cultures in biological researches, we may almost substitute the constituent substances of tubercle bacilli for

those of lepra bacilli. But there is one great difference: tubercle bacilli probably contain a poison, although we find no toxin in those of leprosy. Now I have called these two toxic substances partial antigens, for we were able to prove in the tests for anaphylaxis as well as in the complement-fixation tests that every one of them can form a specific anti-body and also a partial anti-body. It was whilst occupied with these researches that I was first able to show that there are anti-bodies for pure fats.

Now it was further shown in researches on the serum of tuberculous and tubercle-immunised persons that all the partial anti-bodies are not always present. The anti-bodies against neutral fats (tuberculonastin) seem however to occupy the first place, and very often they are generated *sua sponte*.

Quite different are the results obtained from lepers, who have had no previous treatment, for here the fatty anti-body is absent. In this fact we have an important indication as to a new therapy of tuberculosis, as well as a theoretical confirmation of the leper therapy of DEYCKE, discovered by empirical deduction.

Further, if we are to eradicate the disease it is probable that not only one but the whole sum of the partial anti-bodies must be brought into play. We see, for instance, in leprosy, that although there exist already in the blood anti-bodies against lipoids and albumen, we still have to produce the fatty anti-bodies. This we were able to do by vaccine-therapy, namely, by injecting the specific fatty body. This is the method in DEYCKE'S nastin-therapy, and as I have said before, this fact discovered empirically by DEYCKE must now be regarded as a theoretical postulate.

Moreover, the great successes of DEYCKE'S therapy furnish us with confirmation of the accuracy of our researches and conclusions, and further support is supplied from the fact that we are now able to prove that the fatty anti-bodies were previously absent from the blood of those patients who are cured or improved by the nastin therapy. We find in fact a parallel between the appearance of the fatty anti-bodies and the improvement of the leprous process.

The failure of nastin therapy in some cases, indicates too that another partial anti-body is missing, and this fact can also be determined by serological methods.

III.

In concluding and summarising the statements contained in the first chapter, I beg to call your attention to some quite new results in the investigation of leprosy. I was able, for instance, to show in collaboration with LESCHKE that on account of the relationship between lepra and tubercle bacilli we can produce extensive leprous alterations by subcutaneous injection of lepra bacilli in tubercle-immunised animals. This success is due to the fact that, thanks to the same specific substances, tubercle-immunised animals are also anaphylactic against the bacilli of leprosy.

The necessary tubercle-immunisation was effected by a vaccine, which was first made by DEYCKE and myself, by dissolving tubercle bacilli in organic acids. With these substances, which contain no vital material, we were the first to produce tubercle immunity in animals, and that we can now do with great ease.

I wish also, to-night, to direct your attention to the results of our experiments with goats, as they present a very definite and remarkable illustration of our work.

In our first researches the immunised animals were treated with small quantities of lepra bacilli, prepared by antiformin, and probably already dead.

The control animals responded with prompt absorption, while in the treated animals small tumours, the substance of which was indistinguishable from tuberculous tissue, were formed. When these tumours were extirpated, we found in their centres tough dense tissue, and also granulations of typical tuberculous formation with a great many giant and plasma cells. I am able to demonstrate them to you here in my preparations.

In the second series of tests the animals were treated with large doses of bacilli, which were already partly killed. Here large tumours formed which, after increasing to the size of apples, developed into leprous suppurations, practically of a pure type.

In the last tests the animals were prepared with a large dose of lepra bacilli, which were derived from a fresh leproma, and were probably still living. The controls showed total absorption, whilst in animals treated in that way extensive infiltrations, as large as the palm of the hand, quickly developed, and in most cases again became pure leprous

suppurations. The non-suppurating infiltrations were found to consist of granulations with a great many giant cells and characteristic tubercles. Let us see whether the process remains local or is a general infection.

The first important fact to be noted is that the blood of the control animals was absolutely negative to lepra bacilli, while that of the treated animals showed, simultaneously with the fixation of the leper virus, a very strong reaction. Again, the proof that we have produced leprous alterations would not be complete if the chief objection that could possibly arise—viz., a mixed infection—were not disproved. From a superficial point of view it may be said it does not follow that the alterations in the animals are produced by lepra bacilli; possibly they were caused by tubercle bacilli, which were accidentally present in the lepromata along with the lepra bacilli. But this objection may be invalidated by the following considerations :—

(1) It is highly improbable that tubercle bacilli should be present in three lepromata from different patients.

(2) Even if that had been the case, the result would have been just the contrary of what actually occurred—the control would have got tuberculous alterations and the immunised animals have remained free from that infection.

(3) From the pus and small pieces of the tissue no tubercle bacilli could be cultivated on artificial cultures.

(4) Parts of the tissue and pus were inoculated in normal guinea-pigs without producing the faintest trace of tuberculous alterations. Had the new growths been due to tubercle bacilli these animals would have necessarily become tuberculous.

(5) And, lastly, the formation of lepra antibodies in the animals in which these pathogenic changes occurred attests the leprous nature of these alterations.

And with this I submit the proof is complete.

In conclusion, the importance of these results lies in four different directions :—

(1) It is worthy of remark that a micro-organism which produces in a normal animal no pathogenic alterations is able to produce them in a body which has been treated in a special way.

(2) These results demonstrate the relationship between lepra and tubercle bacilli in a somewhat striking but nevertheless a provable way.

(3) And, further, these results affect the dogma, that only a typical tubercle bacillus can produce tubercles. And, certainly, the elimination of a dogma is in itself a good thing. As the lepra bacillus is related to the tubercle bacillus, it is not surprising that it can produce pathogenic alterations similar to those of tuberculosis under artificial conditions, as, biologically, both sorts of bacilli can elaborate partly similar, partly identical substances.

(4) Lastly—and this is the most important fact—it is possible that these results will enable us to produce antileprous substances in animals. Up to now this has been found impracticable, as normal animals have never before reacted to leprosy. It was further impossible, as we have never had animals in which the question of tubercle immunisation was entirely free from objection, and in which immunisation was effected by non-living virus. To show if we can succeed in the therapy of human leprosy with these specific antileprous blood-substances will be the task of our future researches.

NOTE ON SOME EARLY ATTEMPTS AT THE CULTIVATION OF THE BACILLUS OF LEPROSY.

BY

P. S. ABRAHAM, M.A., M.D., B.Sc., F.R.C.S.I.

In the article on Leprosy in Allbutt & Rolleston's "System of Medicine,"[1] I remark that "since its discovery numberless attempts have been made by pathologists to cultivate the bacillus outside the body, but up to the present time without undoubted, absolutely certain, or well confirmed success." I am glad to say that in view of the recent investigations of Dr. BAYON, Captain BEAUCHAMP WILLIAMS and others, this opinion, expressed in 1906, must now be materially altered. In consequence also of what I have lately seen of Dr. BAYON'S work at the Lister Institute, I can no longer agree that "leprosy is strictly a human disease which cannot be transmitted to animals."[2]

From the time when NEISSER demonstrated the fact that the bacillus of leprosy resembled that of tuberculosis in retaining certain aniline dyes after treatment with mineral acids, the attempts at its cultivation have indeed been very numerous. Of course, when the experimenters thought that they had succeeded, they gave to the world their results; but we may safely assume that many other attempts, believed to be unsuccessful, have never been published. In the light of these new and important observations which are now being brought before us, I think we must admit that it is quite possible that some, at any rate, of the older supposed "successful" or supposed "unsuccessful" cultivations were, after all, not absolutely futile, and that the hard and fast criterion of "acid-fastness," which, among others, the critics laid down as a *sine qua non* character of the culture, was really misleading. Having in mind the important observations of Dr. LAWRENCE HERMAN,[3] I ventured to make some such suggestion in the article alluded to above.[4] Dr. HERMAN showed, with material obtained from one of my patients, that "in young or recent nodules, masses of bacilli exist which do not retain the red stain after immersion in weak acid, but are easily subsequently coloured with methylene blue. If, as he supposes, it is only the older (fuchsin staining) bacilli that are resistant to the acid treatment, we may have some explanation of the general failure to recognise leprosy bacilli in the attempted cultivations."

Personally, I have tried on three different occasions to cultivate the micro-organism, but whenever I have obtained a growth it was either an obvious staphylococcic growth, or it did not stand the acid test, and was therefore discarded. My first attempt was made in Professor CROOKSHANK's laboratory at King's College in 1890.[5] Material was taken from three cases of leprosy then in London, and inoculated into a glycerine-agar medium. No growth could be detected in most of the tubes after some weeks' incubation. Some three years later a second attempt was made with a glycerine-agar medium containing a broth made with the skin of a leper at whose autopsy I assisted. In one of the tubes a growth took place, but I did not satisfy myself that it was that of an acid-fast leprosy bacillus, and these observations were also abandoned.

In 1904, Dr. FREMLIN, then working at the Lister Institute, kindly made a number of experiments with bacilli from one of my patients. He tried a large number of media—glycerine skin broth, glycerine skin agar, skin broth, gland broth agar, glycerine gland broth agar, blood (rabbit) agar, glycerine blood agar, blood serum, fish skin broth, fish skin agar, ngapi agar, nga myen broth and nga myen agar. In the note which he has been good enough to give me, he says that "growths of cocci occurred in some of the cultures, and in a few instances bacilli—which were probably 'mesentericus.' In only one case was observed what might have been a growth of lepra bacilli. In this instance, a portion of leprous tissue was mixed with a mass of sterile ngapi. This culture medium was placed in a small glass capsule covered with a lid, and this again inside a vessel holding some water and fitted with a well-sealed lid. The medium was inoculated on April 30th, 1904, and fresh sterile agar added on November 20th, 1904. This, examined on November 11th, 1905, showed small herds of the lepra bacilli, certainly in larger numbers than those observed in specimens from the original nodule. No increase was observed later."

I went to see the specimen, and can confirm what Dr. FREMLIN says as to the greater abundance of the bacilli. This observation practically only confirmed what Dr. ARNING stated in 1890.[6]

Those who are now working at this subject should, I think, particularly bear in mind the observations made by NEISSER in the early eighties, and by Drs. BEAVEN RAKE and BUCKMASTER in India in 1890.

Although endeavours in this direction had been made by MANSON,

HANSEN and HILLAIRET and GAUCHER, NEISSER[7] was certainly the first observer to attempt the cultivation in a thorough manner, and to judge from his account, it is not improbable that, although he did not succeed in cultivating the micro-organisms generation after generation, he did obtain new growths after inoculation in blood serum.

BEAVEN RAKE and BUCKMASTER'S experiments[8] are also not to be lightly passed over. The former observer had previously in 1888, made numerous attempts in Trinidad,[9] without success, but in India, with blister fluid and glycerine bouillon, growths were obtained with comparative ease—which from the description and figures given quite conform to the characters of the lepra bacilli as we know them.

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HUMAN LEPROSY AND RAT LEPROSY; A DISCUSSION OF THEIR RESPECTIVE PROBLEMS.*

By E. MARCHOUX.

Since the discovery by A. Hansen of a specific bacillus in leprous tissue, many authors have published statements that they had succeeded in cultivating this pathogenic germ. Bordoni-Uffreduzzi, Neisser, Babes, Campana, Ducrey, Spronck, Karlinski, Van Houtum, Carasquilla, Deycke, Kedrowsky, Clegg, Twort, Duval, Rost and Williams have all isolated interesting germs of which some were not acid-fast, some became so in particular conditions, and some others completely resisted decoloration by acids. I myself have separated from leprous nasal mucus, in impure cultivations, an acid-fast bacillus, whose characteristics I reported to the Société de Pathologie Exotique in February, 1911.

Besançon, Griffon and Lerredde, E. Weil, and Ch. Nicolle, obtained primary cultivations without succeeding in transmitting the germs which multiplied in the primitive culture.

There are often many microbes, sometimes very different, for the same disease. This is what made some observers say that leprosy was a single clinical entity but that it was caused by different pathogenic agents in different countries. What is the value of this opportunist opinion? I myself think it quite untenable.

Leprosy is an affection always the same; the germs discovered in leprosy all over the world are identical and constant, so that there is no doubt that everywhere it is the same bacillus and the same disease. This multiplicity of streptothrices and of bacilli, considered as specific, tend to make one to believe that nobody as yet has cultivated Hansen's bacillus, and that the etiological agent of leprosy is necessarily one bacillus, and one only. It is impossible to settle the dilemma at present; we are in the presence of an enigma that we cannot yet solve; and though I do not forget the experiments of Suhai, who, by the way, did not succeed in infecting "in series" the dancing mice of Japan, we do not know any animal sensible to leprosy.

* Presented to the meeting but not read, owing to want of time.

With regard to experiments on human beings the results did not, until recently, shed important light, and it will be better to form no decided opinion on this question for the present.

The multiplication *in vitro* of the specific germ of leprosy may be of great use to us; anyone can affirm it, anyone can contest it. The cultivation of KOCH'S bacillus did not lead to progress in the treatment of tuberculosis.

Another question, concerning which there is much discussion, is the question of prophylaxis. There are in the world thousands of lepers, and leprosy still extends. How can we stop this continual spreading of the disease? How can we prevent it from breaking the bounds which now limit it?

Even at the present time Europe is threatened with renewed infection. With closer relations with the colonies and better communications, is it not possible that we shall have amongst us again, as in the Middle Ages, a disease which was so difficult to eradicate. If this sad eventuality should be realized have we any means of defence?

If we study the laws of the countries where leprosy exists, we can see that measures of prophylaxis are still the same as in the Middle Ages.

Beyond isolation of leprous people, practically nothing is done, and what does this isolation entail? Sick people, quite innocent and much to be pitied are condemned to live like prisoners in perpetual banishment. It is hard to believe in our time, when everyone has so great a respect for individual liberty that such methods can be justified, except in certain cases of mental intoxication. Syphilitic and tuberculous patients are a far greater danger to humanity than lepers, yet nobody thinks of burying them all alive.

It is the duty of scientific men to discover the etiology and epidemiology of leprosy and to make its prophylaxis more humane and easier, and the two points of most importance for leprologists are—

1. What is the method of transmission of the disease?
2. How can we prevent its invasion?

I adopted such a plan of inquiry when, four years ago, I began the study of a disease somewhat resembling leprosy. I mean the leprosy of rats, discovered in 1903 in Odessa, by STEFANSKY, and since found in all parts of the world.

The human disease and the disease of rats are caused by germs of the same family; both acid-fast, both probably not capable of cultivation; both specific for the species in which they live; both parasites of macrophages; both more dangerous to the organism by their destructive than by their toxigenic power. Their disposal in the cell is different. The bacillus of man is grouped together in masses, the rudiments are arranged like cigar packets and surrounded by a glutinous envelope. The bacilli of rats are free and spread without order in the plasma cells. This difference is not so important as it seems to be at first, and it may depend on a special reaction of the human cell which contains the parasite. It is far from my belief that human leprosy may proceed from rat leprosy; but no doubt both affections follow the same method of development, essentially chronic and torpid, without marked reaction of the organism and with the same termination, rarely causing death of themselves, man and rat usually falling victims to an intercurrent disease.

I do not wish to further develop this parallel, of which I gave a rough outline before the Société de Biologie, and to which I will return later on, but I wish to keep your attention on the connection between both diseases in order to show you that it is natural, though hypothetical, to believe that there is an analogy in the method of their invasion. However, I think it useful to describe briefly the researches which I carried out, partly with Dr. SOREL, on the etiology of the rat disease, in the hope that doctors who practise in countries where leprosy spreads will bring forward observations which may confirm or contradict my hypothesis.

In Paris, as elsewhere, the leprosy of rats manifests itself under two forms: one purely glandular, in which the infection remains in the superficial lymphatic glands; the other a continuation and aggravation of the first, in which the disease extends to the connective tissue, subcutaneous and intramuscular, an extension which is followed by epidermic necroses and sores, muscular atrophy and troubles of movement.

The primordial localisation of the germs would lead us to believe that they must enter by the skin, but the method of penetration is quite unknown.

Some authors attribute to insects the communication of leprosy, whilst others with great authority deny it.

To obtain information on this point we made investigations on the ordinary parasites of the rat. If biting insects can transmit the disease they must indeed be present wherever rat-leprosy is found, and they must also be there in numbers in proportion to the contaminated rats.

The only parasites of sewer-rats which answered to both conditions were the louse *(Hematopinus spinulosus)*, the acarus *(Lælaps achidnimus)*, and the flea *(Ctenocephalus serraticeps)*, and we studied with great care a large number of these three species of parasites. All of them had in the digestive duct or elsewhere acid-fast bacilli comparable to the leprosy bacillus. In the louse only we found a short and thick bacillus with slight resistance to the action of acids. All the inoculations with it had a negative result.

We did not succeed in transmitting from sick to healthy rats, a great number of each of these anthropods. And the conclusion is that bites of insects are not responsible for the transmission of the bacillus of Stefañsky. I may say here that that accomplished Russian observer himself, who discovered the disease of rats, and Lydia Rabunowitch believed that it was not capable of inoculation, although George Dean, and, after him, McCoy, Alexandescu and others have succeeded in producing experimental inoculation. I cannot understand the failure of the first observers, except that they did not continue their experiments for a sufficiently long time. It takes from four to six months, or even a year, for the disease to declare itself or even for the infection to be noticed.

Rat leprosy is very easy to transmit; not only does subcutaneous inoculation succeed every time, but especially when experimenting on young rats one can obtain 100 per cent. of successes, either by scarification of the epidermis or in spreading with a cotton plug a little of the septic material on depilated skin. The healthy skin of quite young rats, some days old, stops the germs, but it is sufficient to contaminate a healthy rat by simple contact when there is only a slight erosion of the skin with the pathogenic germs which are always found in great numbers in leprous sores. These conditions, without any doubt, are realised frequently in the great proportion of sick rats.

In Paris the inguinal glands are first affected, and I consequently thought that the route of introduction might be by the genitals, and very often one found bacillar nodes in the vulvæ of females. In one of

our experiments the bacilli of STEFANSKY were simply put into the genital sheaths of two males which were placed in a cage with four females, and kept with them for one year. After that time the animals were killed. The two males had inguinal glands crowded with bacilli, the females were unaffected.

This experiment shows that if my hypothesis is correct bacilli simply placed on a healthy mucous membrane can spread to the lymphatic ducts.

Another result seems to me important. Out of 1,296 Parisian rats that we examined, 65, that is to say, 5 per cent. were carrying acid-fast bacilli; 9 only had clinical signs of leprosy, that is to say, 0·69 per cent. on the total number of the animals; and 15 per cent. were bearers of germs. We infected artificially about 300 rats; two only after one year were leprous, which gives only 0.66 per cent. of cases of regular development of the disease in animals certainly contaminated. In a great number of rats the infection remains for a long time, and perhaps is fixed in the organism, but is ready to burst out if animal resistance is diminished.

To sum up, the result of these experiments is:—

1. That the bacillus of the rat can be readily transmitted by the skin when it is slightly eroded and by healthy mucous membrane.

2. That it seldom produces an affection capable of being diagnosed during life.

Can both these conclusions be accepted in regard to human leprosy? It is probable that they may.

In the Middle Ages hygiene was so primitive that the transmission of leprosy by contact was quite easy. Cleanliness was very doubtful and promiscuity was great. People had no repulsion to use the same bed or clothes of a stranger. In the hospitals there were eight patients in the same bed.

In the present time there are still lepers in London. In Paris there are two hundred living with other people and not isolated. In some hospitals for fifty years lepers have lived in the same place with other patients, but had their own bed and clean clothes. We have never known, in town or in the hospital, an autocthonous case of leprosy.

I recently had the opportunity, with Dr. BOURRET, to visit an actual centre of leprosy. In a very dirty house we found four persons, a mother

and three children—two girls of age and a boy of seventeen. One of the two sisters had recently contracted leprosy, and both used the same bed, and what a bed! A truckle-bed with sheets more black than white, and which had not been changed for a long time. The mother had symptoms of nervous leprosy, and she slept with her son in a filthy loft.

This exhibition of three different social conditions is sufficient, I think, to justify the hypothesis of transmission by contact.

I could easily talk longer on this subject, and give many examples to prove contagion by direct contact, but it is now a matter of common knowledge. Here I might call attention to the danger for laundresses, whose hands are softened and liable to get the germs.

One of the most surprising phenomena in the history of leprosy, and one which seems to throw doubt on the theory of contagion, is the selection that the disease seems to make of its victims. Only certain people seem capable of infection. Conjugal leprosy is rare, but according to SAND, 5 to 10 per cent. of leper's children become lepers. Sometimes one observes a sporadic case without apparent heredity, but if some trouble be taken ancestral leprosy can generally be discovered.

Is it not probable that in man, as in the rat, the specific bacillus is transmitted more easily than one imagines, but it is no doubt the case that the diagnosis of the affection is manifest only in a small number of cases, nearly in the same proportion in human beings as in rats. There only post-mortem researches will help us.

THE PRESENT POSITION OF THE LEPROSY QUESTION.*

BY SIR JONATHAN HUTCHINSON, F.R.S.

I have been much gratified by an invitation from the Society of Tropical Medicine that I should write a paper at the present juncture on the subject of leprosy. Little more than two years have elapsed since the second international congress on this subject was held at Bergen, and this invitation given to myself I understand to imply, since my opinion is well known, a certain degree of approval of it. It must be confessed that neither of the two congresses have marked any definite progress, and they certainly did not chronicle any remarkable observations. The facts in reference to HANSEN'S discovery of the leprosy bacillus have, of course, been confirmed, and universally accepted, and strenuous endeavours have been made to discover their practical applications. Their investigation has indeed been permitted to somewhat withdraw attention from all other directions of research. Accepting the facts concerning it as a basis, we may, I think, narrow the leprosy question—as indeed it has been narrowed for the last twenty years—to the determination whether the disease is originated and spread chiefly by personal contagion or by personal habits of diet.

To begin with Norway. It is unquestionable that the progressive and even rapid diminution of the prevalence of leprosy on the west coast of Norway, and its promised extinction there, has been by far the principal fact which has attracted popular attention, since it has coincided with the enactment of laws and the zealous advocacy of the doctrines of contagion.

In order to avoid being diffuse, I must be explicit, and must state at once that, if fairly investigated, the facts do not seem to me in the least to support the doctrine of contagion, but emphatically the reverse. An important paper read at the last congress demonstrated that the decrease and almost extinction of leprosy in Norway was occurring now not for the first time, but was a repetition of what happened more than a century ago when the disease was recorded as having almost died out, and that its prevalence in the middle of the last century was a recrudescence which has subsequently resulted as we know in its more recent decline. We

* Presented to the meeting but not read, owing to want of time.

know nothing as to the cause of the first. I can only remark that it was coincident with a similar reduction of the malady in many other parts of Europe. In some of these it has not returned, whilst in others it still persists. In the British Isles, for instance, it very gradually diminished, and, as is well known, at the present time it is almost extinct. The history of its decline and the apparent impossibility of effecting its re-introduction to any appreciable extent are, I submit, conclusively opposed to any belief in transmission by personal contagion. During recent years, throughout Great Britain, leprosy has occurred only in sporadic instances, one here and one there, almost invariably in those who had lived elsewhere and in leprosy districts. No laws have been enacted, and no social precautions have been insisted upon in order to prevent its spread—but the disease will not spread, and in the exceedingly few instances which have at first sight seemed to imply contagion, the evidence has usually been very flimsy. From no part of Britain are lepers excluded at the present day, nor is there the slightest impediment offered to their dwelling amongst us in any capacity which they may select, or travelling by our public conveyances wherever they may choose to go. All that is necessary is that the disease should be concealed from the public. To turn to foreign parts, no new facts definitely implying contagion have been brought to my knowledge. Experimentalists in search of proofs of contagion have, I think, in like manner failed of results. Painstaking investigation has been made as to the possibility of transmission by insect bites, etc.

It is of course easy enough to produce instances of supposed contagion in districts where leprosy prevails, but to these the reply is obvious that it is at the same time possible that they are examples only of dietetic production. What we want are cases in which dietetic causation is reasonably excluded, whilst exposure to so-called contagion has been definite.

The fact that leprosy occurs in certain communities in which fish is not abundant and which are at a distance from the sea coast and rivers, has been a stumbling block to many, and it was so, if I mistake not, in Kashmir to Dr. Neve, who observed it was not merely in the dwellers on the borders of the lake, but in the dwellers in mountain regions who were not fishermen but shepherds, that the disease chiefly occurred. This fact has been observed in many districts, and I have repeatedly

tried to impress as an obviously possible explanation that it is at places distant from fisheries that badly preserved fish is most likely to be eaten. The shepherd or farm labourer pursuing his occupation at places distant from his supplies, is precisely the person not unlikely to provide himself with half-cured fish, and the fact is that he habitually does so.

Dr. NEVE's observations on the hill districts of Kashmir and those of a similar character, so far from being in opposition to the fish hypothesis, are precisely those which confirm it.

During my journeys in the east, in search of leprosy facts, I was frequently advised—more especially by army medical men—that I ought to go to Burma. Now undoubtedly Burma is a home of leprosy, but it did not present for me the essentials of any problem, for the facts were only too conspicuous and in favour of the fish theory. Burma is not only a home of leprosy, but the Burmese are notoriously a fish-eating people. They are indeed precluded from almost all other articles of animal food. They will not take the life of any animal and are very strict in their religious observances, but the cold-blooded and lifeless fish is regarded as only half an animal and obtains no immunity. Thus in Burma we not only have the risk of the possibility of fish production, but several of its possible competitors are excluded. In South Africa, both Kaffirs and Hottentots will eat flesh meat in a decomposing condition, whilst only in some parts of the district have they much access to fish.

Leprosy occurs amongst them and by some observers rotten meat has been suspected. It is very widely prevalent amongst the Burmese, however, whilst it is only occasional amongst the Kaffirs. Amongst the Burmese fish is the only animal food open to suspicion.

Not only however is it well determined that in all parts of the civilized world isolated cases of leprosy have been admitted and allowed to reside without impediment, but that no instances of anything approaching to epidemic prevalence have originated from them. I am entitled, I think, to assert that during the last twenty years I have made similar statements in the most definite manner, and that they have elicited no contradictions. Lapse of time and publicity have, I think, done much to substantiate the conclusion which is, I believe, becoming increasingly prevalent to all careful observers that leprosy, if a contagious disease at all, becomes so only in the most exceptional instances.

If then we may assume it to be proved that transmission by personal

contagion is no more supported by recent observations than it was at the time of the writing of DANIELSSON and the reports of the College of Physicians, and the expressed opinions of a whole multitude of medical observers, we may next ask how the question stands as to the possibility of diet.

I should weary the Society if I attempted to quote evidence in proof of the fact that all over the world and in all times which have a history, the prevalence of leprosy has appeared to be coincident with the liberal use of fish as food, or what is equally important, with its occasional employment in bad conditions of preservation, I have drawn attention as conspicuously as I can, indeed I have almost advertised it, to the fact that leprosy is met with very frequently in the southern and fish-eating regions of China, whilst it is almost unknown, although the race is the same, in those of the north.

I have challenged any explanation of this as other than resulting from the fact that in the south much fish is consumed and salt is dear, whilst the exact reverse is true of the north. Now, although a willingness to confute the fish theory of the disease has not been wanting, yet I am not aware that anyone has attempted an answer to my challenge in this respect, and I do not believe that one can be given.

In a contribution to the *British Medical Journal*, in reference to the suggestion made by authorities in Robben Island and in Basuto Land, that bed bugs may possibly communicate leprosy, I have done my best to discredit that hypothesis. The facts which they adduced in reference to it never amounted to more than a suggestion of possibility. It had in fact been very much discredited in anticipation by the elaborate experiments of Dr. EHLERS.

The special conditions under which leprosy has finally been extinguished in many districts are well worth more detailed consideration than they have received. In Norway, at the present time, this extinction is believed to be taking place, and its final extinction is confidently foretold. Now, on the theory that it is a contagious disease, what ought to be the course of action of those responsible? Clearly, I think that they would be most zealous to place under control in strict isolation all the remaining sufferers from it; and every effort would be made to compel all sufferers to isolate themselves. The more reduced became the numbers of them, the greater would be the zeal to accomplish its complete extermination.

Instead of that, we appear to observe only increased confidence in its spontaneous disappearance. Every year less and less is done in the way of isolation ; and what is occurring to-day in Norway, is exactly what has occurred in almost all countries from which the disease has finally disappeared.

On the theory that the efficient cause of leprosy is personal contagion, I can scarcely believe that its complete extinction from any locality in which it had once prevailed would be possible. It is a malady so chronic that the period of proneness to its communication must extend in most cases over many years. Nothing but the most rigorous and efficient methods of isolation could possibly prevent it. However much it might be reduced in prevalence by such methods as have been adopted, there would still always remain a few cases, embers as it were from which the fire might be re-lighted. It would certainly be the duty of those resident in districts in which such remarkable diminution had occurred, or was in apparent progress, to use every effort to stamp out those embers. We may profitably direct our attention carefully to the question whether in any instance such precautions have been adopted. In order to do this we ought to investigate very scrupulously the facts under which leprosy in any district has, after declining to a minimum, eventually become extinct. Plenty of such may be had for searching, and I unhesitatingly assert that measures of the kind referred to have almost invariably been conspicuously absent.

The decline of leprosy in any district in which it has once been prevalent, is usually accepted with pious feelings of gratitude to God, and at once the troublesome expedients to secure isolation have been diminished. We may take as an illustration of this what has twice occurred in Norway. It is on record that on the partial disappearance of the disease more than a century ago, the leper houses were almost closed. The same practice has been followed during the very remarkable diminution of the malady which is at present going on ; yet I would submit that it is precisely the opposite to that which is most desirable. If we might suppose that a disease which spread solely by contagion had been reduced to such an extent that only six individuals suffering from it remained in the whole population, those six ought surely to be most carefully secluded. It can scarcely be denied that where the disease is not very prevalent, the proportion of those subject to isolation in

asylums is a fair test of the general zeal for preventing contagion, and gives us a fair estimate how so far from an increase in the total of those secluded, having been in increased ratio to the population in Norway during the last half century, it has been precisely the reverse. Instead of its having been accepted as an opportunity of its final extinction by vigorous measures, the number of leper houses has been diminished, and the ratio of those confined in them has been progressively diminished.

With the greatest possible respect for those engaged in the practical management of leprosy in Norway, I submit that the measures that they adopt are not consistent with the real belief that the disease spreads only or principally by contagion, and that they are not likely to obtain the result they desire.

My own still persisting conviction, as the result of steadily accumulating facts, is the belief in the dietetic causation of leprosy, and that the special dietetic element is badly cured fish.

The PRESIDENT expressed the special thanks of the meeting to those who had contributed papers, and particularly to Professor DEYCKE and Dr. MUCH, who had come over from the continent in order to take part in the meeting.

DISCUSSION.

Dr. MCLEOD: In the first place I must congratulate Dr. BAYON very heartily on his work. I have had the pleasure of watching the various stages of his research at the School of Tropical Medicine, and it seems to me that the acid fast streptothrix which he has succeeded in cultivating, is most probably the casual micro-organism of leprosy.

With regard to the identity of human leprosy and the rat disease, his experiments are most suggestive.

I have also been much interested in Professor DEYCKE's description of the results he has obtained with nastin. In this country the cases of leprosy are fortunately insufficiently numerous to enable us to give the remedy an extensive trial. In the cases I have treated with it I have not been convinced of its value. In one case of nodular leprosy in which it was employed according to the rules laid down by Professor DEYCKE, the disease in spite of a year and a half's treatment with nastin, got

steadily worse. In another case of the maculo-anæsthetic type, which has been under nastin treatment since 1909, no definite change has occurred. There is also the great practical difficulty of coming to a conclusion with regard to the merits of a new remedy for leprosy, unless by it the objective symptoms can be cleared up in the same dramatic way that syphilitic manifestations sometimes disappear after an injection of salvarsan, because it is in the nature of the disease to undergo periods of remission and exacerbation apart from treatment except on ordinary hygienic principles. This is especially noticeable in cases of leprosy which come to live in countries where the disease is no longer endemic.

Dr. A. G. FOULERTON : As a visitor I am grateful for having had the opportunity of hearing the contributions of Professors MUCH and DEYCKE, both of whom have done such valuable work in connection with the acid-fast group of organisms.

In discussing the papers which have been read there are three questions to be considered : (I) What is the exact nature of the parasite of leprosy ? (2) What is the probable value of the treatment of leprosy by bacterial vaccines? (3) If treatment by a bacterial vaccine is advisable, is nastin, a separated constituent of the parasite, preferable therapeutically to a bacillary vaccine made from the whole organism, such as the bacterial vaccine which has been used by Capt. BEAUCHAMP WILLIAMS ?

It is scarcely necessary to elaborate an answer to the first question. From the time when DEYCKE isolated and described *streptothrix leproides*, which he obtained from leprous lesions, and from which nastin is prepared, many of us have accepted an acid-fast streptothrix as being the causative parasite of leprosy. But the credit of proving conclusively, by the ordinary methods of bacteriologists, that a streptothrix is, in fact, the cause of leprosy, is due to Capt. BEAUCHAMP WILLIAMS, whose first paper on this question was published by the Indian Government in, I believe, September, 1910. And, with reference to this, I feel compelled to say that the published work of the two officers of our Indian Medical Service—Major ROST and Capt. BEAUCHAMP WILLIAMS—who have done more than any others since HANSEN to increase our knowledge of the parasite of leprosy, has not been justly appreciated by some who have written on the subject recently. ROST announced, nearly simultaneously with DEYCKE, that he had isolated the causative parasite of

leprosy. Whether DEYCKE's or ROST's announcement was published first is not a matter of very great importance. But, in any case, it seems to be certain that ROST was the first who succeeded in growing the parasite of leprosy quite freely on ordinary culture media. ROST did not recognise his culture as being that of a streptothrix; and others, finding diversely formed elements in ROST's cultures, and not understanding the morphology of various forms of streptothrix, concluded that the cultures were badly contaminated with extraneous micro-organisms. We know now that ROST's original cultures obtained from a case of leprosy were actually pure cultures of a streptothrix. BEAUCHAMP WILLIAMS has proved this fully; he found that ROST's bacillus of leprosy was identical with the organism which he himself isolated, and recognised as being a streptothrix.

This question as to the exact nature of the parasite is not merely academical; it has a near relation to any decision with regard to treatment by a vaccine. It is important to know whether the specific parasite is a uniformly acid-fast bacillus, as believed by HANSEN, or whether it is a streptothrix, whose acid-fast forms represent merely one phase of its growth.

The second question, as to the actual value of the treatment of leprosy by a vaccine—whether the nastin of DEYCKE or the bacterial vaccine of BEAUCHAMP WILLIAMS—cannot be answered decisively at the present time. In the case of a chronic infective disease, such as leprosy, the apparent results of treatment require very careful control by a large number of observers. We are without any precise knowledge as to the occurrence of self-arrest in the disease under natural conditions, and apart from special treatment. Isolated cases of improvement under one or other form of treatment are hopeful; but much more accumulation of evidence is required before we can speak of the vaccine treatment as being successful.

But, judging by analogy with other chronic infective diseases, there is good reason to believe that treatment by bacterial vaccination is that which holds out the best prospect of cure. And that being so, we have to decide, and the decision must be come to mainly on theoretical grounds since there is not sufficient clinical experience to rely upon, as to the probable relative values of the vaccines available—the nastin of DEYCKE and the "whole" bacterial vaccine which BEAUCHAMP WILLIAMS

advises. The admirable work of Professor MUCH and his colleagues in Hamburg has shewn that the neutral fat, nastin, isolated from *streptothrix leproides* of DEYCKE is a constituent common to the acid-fast forms of the parasite of leprosy, of the parasite of human tuberculosis, and of several other acid-fast species. And consequently when nastin is used for immunising purposes one can expect only the production of a "group" antibody, and not one which is strictly specific for the parasite of leprosy. But more than this, the acid-fast forms of a streptothrix represent only a single phase in the life of the organism. Young cultures are not acid-fast; the property is one which is acquired in later growth, and even then is, under the conditions of culture on artificial media, of very variable occurrence. In a sense, the acid-fast phase of a streptothrix is an accidental one: the acid-fast type probably representing more resistent forms of the organisms. And it is certain that nastin, as an antigen representing a special, and more or less accidental constituent present only in the parasite at a particular stage of its growth, cannot be expected to excite the production of antibodies, which would be in any sense specific for the younger non-acid-fast forms. On the other hand, the "whole" bacterial vaccine of BEAUCHAMP WILLIAMS contains, in addition to the fatty antigen, the specific protein antigen necessary for the production of antibodies strictly specific for the parasite at all stages of its growth. For this reason, the "whole" bacterial vaccine would appear the more suitable for therapeutic use.

With reference to the contribution of Dr. BAYON on the possible relationship of human and rat leprosy, one notices the omission of any details as to the cultural characteristics of the parasite which was isolated from the rat, and so it is not possible to form any opinion as to whether the organism which has been isolated from cases of rat "leprosy," or "tuberculosis," is the same as that isolated by DEAN and others. Reliance appears to have been placed on the serological tests. But in view of the researches of MUCH, which prove the existence of "group" fat-antibodies, as well as strictly specific antibodies, in the serum of hosts of acid-fast parasites, it is advisable that the results of complement-fixation tests should be carefully checked by other more simply interpretable methods.

Dr. GEORGE TURNER: I should like to congratulate Dr. BAYON on his work. He was kind enough to show me his results the other day, and to my mind they are most convincing.

I think Major ROST hardly had justice done him when he first announced he had succeeded in cultivating the bacillus of leprosy. At the time I wrote, in his defence, to the *British Medical Journal*. Even if he had made a mistake, he is not the first and only man who has done so, especially in connection with leprosy.

I have the greatest respect for bacteriological work, and have no wish to minimise the importance of the results obtained in the laboratory. To do so would be foolish. Still, I think you will all agree with me that for a final and authoritative estimate of the value of any method of treatment we must appeal to clinical medicine.

When dealing with a new drug or a new process we want to know how it will work out in a human being, not in a test tube or a rat.

Professor DEYCKE is apparently of that opinion since he brought to our notice the results obtained by the use of his preparation and method in a large number of leper patients.

Very wisely, too, he relies principally on figures supplied by others, *i.e.*, he shows us what can be done by the general practitioner as distinguished from the expert.

Unfortunately, the way in which it has been attempted to show the benefits conferred by the use of nastin could not possibly furnish a reliable answer, unless indeed all or nearly all the cases treated had been cured or arrested.

The figures just displayed on the screen showed that $2\frac{1}{2}$ per cent. of the patients who underwent the course of treatment might be described as cured, or the disease was in their case arrested.

If, however, you have the opportunity of treating many hundreds of lepers, you will find that in from 2 to 3 per cent. of your patients the disease will become arrested or cured without any specific treatment whatever.

To answer the question: "Do patients derive more benefit from the use of nastin than from any other treatment?" two series of cases, of average similar severity, should have been taken. The one should have been submitted to the influence of nastin, while the other should have been injected with some indifferent fluid, in order to keep the patients in

ignorance of the fact that they were not undergoing the "new treatment."

I employed this method in testing the value of a drug at Pretoria. Fifty patients took the drug and fifty others were given a mixture of lime juice, syrup and tincture of ginger.

The results were precisely similar; in fact the glorified ginger beer was supposed to produce such wonderful effects that it was kept in stock.

Unless, as I said before, the cures or arrests very greatly exceed 2 to 3 per cent., the figures obtained without control mean absolutely nothing.

With respect to the results described as "nearly cured," "much improved," "improved," "not improved" and "dead," the personal equation enters so largely into the classification, that with the exception of those in the last category, no reliance can be placed on them.

I have passed between six and seven years in a leper asylum and have had nearly five hundred lepers under my care at one time, and in less than twelve months I learned that leprosy was a very deceptive disease.

I have seen a leper, a white man, well able to do a day's work on the farm. He ran away to his home in the veldt, and remained away some five or six months until he discovered himself to the police and was sent back to the asylum.

When he attended at my consulting room for re-examination on re-admission, he was brought to me in a barrow as he could not walk. He was given good food, was well clothed, regularly bathed, and his sores were dressed, but he did not receive any specific treatment. In a month or two he was about again and soon resumed work.

It was very easy for patients to escape from the Pretoria asylum, and many of them availed themselves of this opportunity, especially new cases. The majority were re-admitted, either because they returned of their own free will or were taken by the police.

My experience was that, provided they remained out long enough, *i.e.*, two or three months, they returned in a much worse condition than when they escaped, and that almost invariably they picked up, put on flesh, and gained strength under the simple influence of cleanliness, rest and good food.

And in weighing the results put before us, it must be remembered that all patients undergoing treatment, either by nastin or any other

remedy, must necessarily come under the frequent and minute observation of the doctor and the nurses, consequently immediately an ulcer or any other accident supervened they would be promptly treated, and they would be kept scrupulously clean.

I do not know what may occur in other asylums, but I know that at Pretoria, patients, unless closely looked after, delayed coming to the surgery to be dressed until they were obliged to do so, and this would tend to vitiate any comparison drawn between patients treated and ordinary patients.

I hope and believe we can now cultivate the bacillus-lepræ, and can produce leprosy in the lower animals, and this is a great step towards obtaining a method of cure.

Fortunately, leprosy is not the necessarily fatal disease it was supposed to be. I have known patients who have been lepers for years, one for nearly forty years; often years have elapsed without the appearance of any active leprotic symptoms. Of course, in consequence of anæsthesia they were very liable to burns, scalds and other accidents.

I may add that leprosy is a disease in which I have been keenly interested since 1895, when I was first officially connected with Robben Island.

Sir Arthur Downes: I cannot, I fear, add anything that will be of interest to the meeting to-night, and I regard leprosy from a somewhat different standpoint to that of the papers before you this evening. My interest is rather from a social point of view, the view of Public Health and Public Assistance, and I have come here to night rather as a hearer. The difficulty in England of dealing with leprosy is to some extent due to the comparatively small number of cases we have. From the point of view of the State it is easier to deal with large numbers, but as the centre of a great empire, with fruitful fields for this disease in India and the Colonies, and with the ever-increasing facilities of transit, we must expect to have a fair number of cases finding their way to us. Therefore I do not think that we can altogether leave the question outside the pale of our Public Health measures. Of this, however, I am not entitled to speak, as I am connected with the Public Assistance rather than the Public Health side of the Local Government Board. From the Public Assistance point of view these cases especially appeal to us for consideration.

I have had occasion to see a considerable number of these poor people in past years, and in the past twelve months I have seen a fair number. I have seen them in their houses, afraid to stir out, many of them not destitute of the means of a fairly comfortable existence, but unable to provide for themselves from their own small means the special requirements of nursing or of segregation, which this formidable disease imposes upon them. And the dread amongst the population, probably from the Biblical tradition of Gehazi, is so great, though out of all proportion to the actual danger, that they tend to be regarded as pariahs. If by chance a case is brought into a hospital, and it transpires that it is a case of leprosy, he may have to be removed from the hospital, in which event there is nothing left for him but the poor law and the workhouse, where there is no suitable accommodation.

These are problems which need to be faced, and I hope that it may be possible to provide by voluntary effort some accommodation on a moderate scale, and so arranged that it will not prove a temptation to lepers from other countries. If so it might afford not only a refuge to the sufferers, but may assist the research which we wish to carry on in this country into a disease which affects us as an empire.

Dr. H. Bayon: I was very pleased to hear that Dr. Much has quite independently confirmed several points of my work.

Regarding the group reaction caused in acid-fast germs by their "Nastin" coating, I believe that I have shown how it can be got rid of, viz.: by systematically varying the proportions of antigen and serum. The complement absorption tests shown were absolutely specific. There is another way of getting rid of the group reaction, and that is by previous absorption of the group anti-body, filtration with following titration of the serum against its homologous antigen. I have not yet made use of this method because the one demonstrated was sufficiently exact.

Another observation Dr. Much made was that apparently dead acid-proof germs are capable of producing lesions very similar to those brought about by living germs. I projected a slide to show this very same result.

In previous papers of mine I mentioned the fact that Dr. Much's investigations so clearly demonstrate, *i.e.*, that the germ of leprosy

resembles the tubercle "bacillus" less its toxine. The reaction caused by the injection of leprous nodules in goats immunized against tubercle, is extremely interesting.

Regarding the remarks of Dr. FOULERTON, I can say that I was not convinced that leprosy was due to a branching germ till I had carried out the experiments myself and had sufficient proof to state a case on my own evidence. I believe that he has misunderstood me. What I said in my first paper was that I only so far had proof that leprous lesions could be caused by a diphtheroid germ.

Now I think that I can state and prove, as much as our present bacteriological methods allow, that leprosy is caused by a definite branching germ, the various stages of which I have demonstrated, and followed up one by one. Much of my work has been but the confirmation of what had been done before, and time can only show which of the various cultures is the right one.

With reference to rat-leprosy, I must say that I only got the culture a few weeks ago. I have been putting it into guinea-pigs, rats and birds, but cannot expect a result till months have elapsed. It is true I have not identified the germ so far, but as I got it from a rat, which had been inoculated with rat-leprosy, and showed the lesions of rat-leprosy, and as the germ was regained in pure culture from the spleen and is morphologically identical and gives the identical staining reactions of the "bacilli" in the corresponding sections, I am at loss to find out what more could be done for the present. Many germs have been published as being the cause of leprosy with much less evidence. I have been very guarded in my statements and also in this case time only can show whether I am right or wrong.

Regarding the remarks of Sir ARTHUR DOWNES, I have to thank him for the help he has given me in my investigations. I have accompanied him to the addresses of various cases of leprosy in the East End, and can only confirm that it is truly a terrible sight to see in what circumstances these unfortunate lepers have to live. Some of them are quite educated people (one is a mathematician), and their condition is most pitiable as they are shunned by everybody. I think that steps could be taken to segregate them in such a fashion that they could live their lives in comparative repose as human beings, and not as hounded animals as at present.

Professor DEYCKE, in reply, exhibited a number of photographs illustrating the beneficial effect of treatment by nastin, also some diagrams showing the effect of the same treatment upon cases of anæsthetic leprosy.

Dr. ABRAHAM: I should like to say I have had a few cases of leprosy under the nastin treatment, with varying results. One case was an extremely advanced one. The poor fellow thought it was doing him good, but he was dead within the year with advancing ulceration. Leprosy permeated the whole of his system.

Of two other cases, one is now in an infirmary, a poor boy who is quite blind. He is certainly improving under nastin treatment, the symptoms have diminished.

Anyone who has had experience with leprosy will agree that cases may sometimes appear to do well under ordinary hygienic and Chaulmogra oil treatment. I have had myself cases that I thought were almost cured. In one instance the patient lost all the superficial lesions, but they soon started again, gradually got worse, and he went back to his country, British Guiana, where he died shortly afterwards. I have indeed seen several cases, nearly or apparently cured, break out again. On the other hand, I have known cases where the disease has been really arrested for many years, the patient subsequently dying of other complaints or old age, but not of leprosy. One must be very careful when speaking of a cure unless there has been a long time in which to judge.